

Attorney Docket No.: KUZ-0022  
Inventors: Ito et al.  
Serial No.: 10/527,710  
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#### REMARKS

Claims 1-5 and 8-20 are pending in the instant application. Claims 1-5 and 8-20 have been rejected. Claim 1 has been amended. Support for these amendments is provided in the specification, for example, in Examples 1 through 4 beginning at page 13. No new matter is added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

#### **I. Rejection of Claims 1-5 and 8-20 under 35 U.S.C. 112, first paragraph**

Claims 1-5 and 8-20 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Specifically the Examiner suggests that the negative proviso that the instant adhesive patch does not contain an organic acid salt constitutes new matter because some of the hydrophilic polymers listed are organic acid salts.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended the claims to delete this negative proviso. Instead, the claims have been amended to recite the negative proviso that the

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adhesive patch does not contain sodium acetate. Support for this amendment is provided by the specification which the Examiner confirmed during the Telephone Interview via searching of the published patent application does not teach or suggest inclusion of sodium acetate in the adhesive patch of the instant invention.

Withdrawal of this rejection is therefore respectfully requested.

## **II. Rejection of Claims under 35 U.S.C. 103(a)**

Claims 1-3, 8, 9, 11, 12, 14-16, 19 and 20 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Chono et al. (U.S. Patent 6,139,866), Tsuruda et al. (CA 2 424 579), Hirano et al. (U.S. Patent 6,495,159), Higo et al. (U.S. Patent 5,866,157) and Grond et al. (Clinical Pharmacokinetics 2000; 38 (1):59-89).

Claims 4 and 17 have also been rejected under 35 U.S.C. 103(a) as being unpatentable over Chono et al. in view of Tsuruda et al., Higo et al., Hirano et al. and Grond et al. as applied to claims 1-3, 8, 9, 11, 12, 14-16, 19 and 20 and further in view of Urquhart et al. (U.S. Patent 4,031,894).

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Claims 5 and 18 have also been rejected under 35 U.S.C. 103(a) as being unpatentable over Chono et al. in view of Tsuruda et al., Higo et al., Hirano et al. and Grond et al. as applied to claims 1-3, 8, 9, 11, 12, 14-16, 19 and 20 and further in view of Scholz et al. (U.S. Patent 5,750,136).

Claims 10 and 13 have also been rejected under 35 U.S.C. 103(a) as being unpatentable over Chono et al. in view of Tsuruda et al., Higo et al. and Hirano et al. and further in view of Zafforini (U.S. Patent 3,598,122) and further in view of Kochinke (U.S. Patent 5,350,581).

Applicants respectfully traverse these rejections. Applicants have amended claim 1, from which all other pending claims ultimately depend, to include the proviso that the adhesive patch does not contain sodium acetate. Support for this amendment is provided by the specification which the Examiner confirmed during the Telephone Interview via searching of the published patent application does not teach or suggest inclusion of sodium acetate in the adhesive patch of the instant invention.

In contrast, the primary reference cited in all of these obviousness rejection, Chono et al., requires

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inclusion of sodium acetate. See teachings throughout Chono et al., for example, in the Abstract, col. 1 line 64, col. 2, lines 2, 9, 14 and 18 and col. 3 lines 21-32. Clearly exclusion of this required element of Chono et al. renders the instant claims unobvious over Chono et al.

Secondary references of Tsuruda et al. (CA 2 424 579), Hirano et al. (U.S. Patent 6,495,159), Higo et al. (U.S. Patent 5,866,157), Urquhart et al. (U.S. Patent 4,031,894), Scholz et al. (U.S. Patent 5,750,136), Zafforini (U.S. Patent 3,598,122), Kochinke (U.S. Patent 5,350,581) and Grond et al. fail to remedy deficiencies in the primary reference.

The Examiner suggests at page 9 of the Office Action that Higo et al. discuss reasons for why the ordinary skilled artisan would have been inspired to avoid using organic acid salts and Hirano et al. and Tsuruda et al. do not use organic acid salts in the fentanyl patches.

Applicants respectfully disagree with the Examiner's characterization of the teachings of these references.

With respect to Higo et al., the Examiner suggests that column 2, lines 5-22 of Higo et al. teach that the inclusion

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of such salts [organic acid salts] causes irritation at the time of release and insufficient quantities of drug to be released. It is respectfully pointed out, however, that teachings at col. 2, lines 5-22 of Higo et al. actually relate to organic acids, not organic acid salts or sodium acetate.

Organic acids have different chemical structures and completely different properties and functions from organic acid salts.

For example, acetic acid is an organic acid while an organic acid salt of acetic acid is sodium acetate, also commonly referred to as sodium ethanoate. The molecular formula of acetic acid is  $C_2H_4O_2$ . Its molar mass is 60.05 g mol<sup>-1</sup>. Acetic acid is a colorless liquid with a melting point of 16.5°C and a boiling point of 118.1°C. It is fully miscible in water. Acetic acid is an important chemical reagent and industrial chemical, used in the production of polyethylene terephthalate mainly used in soft drink bottles; cellulose acetate, mainly for photographic film; and polyvinyl acetate for wood glue, as well as synthetic fibers and fabrics. In households, diluted acetic acid is often used in descaling agents. In the food industry, acetic

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acid is used under the food additive code E260 as an acidity regulator and as a condiment. Pure acetic acid and its concentrated solutions are dangerously corrosive.

In contrast, the molecular formula of sodium acetate  $\text{C}_2\text{H}_3\text{NaO}_2$ . Its molar mass is  $82.03 \text{ g mol}^{-1}$ . Sodium acetate is a white deliquescent powder with a melting point of  $324^\circ\text{C}$  and a boiling point of  $881.4^\circ\text{C}$  in its anhydrous state and a melting point of  $58^\circ\text{C}$  and a boiling point of  $122^\circ\text{C}$  in its trihydrate state. Solubility of sodium acetate in water is  $36.2\text{g}/100 \text{ ml}$  at  $0^\circ\text{C}$ . Sodium acetate is used in the textile industry to neutralize sulfuric acid waste streams, and as a photoresist while using aniline dyes. It is also a pickling agent in chrome tanning, and it helps to retard vulcanization of chloroprene in synthetic rubber production. Sodium acetate may be added to foods as a seasoning.

Thus, teachings of Higo et al. at col. 2, lines 5-22 of relating to organic acids are irrelevant to exclusion of structurally and functionally different organic acid salts and in particular sodium acetate as now claimed. According, contrary to the Examiner's suggestion, Higo et al. does not provide any motivation for exclusion of organic acid salts, and in particular sodium acetate as now claimed.

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Applicants also respectfully disagree with the Examiner's characterization of Hirano et al. as teaching a fentanyl patch.

Hirano et al. relates to transdermal preparations containing serotonin receptor antagonist. Nowhere does Hirano et al. teach or suggest use of fentanyl in a patch.

Applicants also disagree that Tsuruda et al. can provide motivation for exclusion of sodium acetate in the instant invention as this patent application is also unrelated to adhesive patches for maintaining a long-term drug efficacy of fentanyl for more than 48 hours. This patent application is focused upon imparting ultraviolet shielding properties to a substrate of an adhesive preparation.

Secondary references of Urquhart et al. (U.S. Patent 4,031,894), Scholz et al. (U.S. Patent 5,750,136), Zafforini (U.S. Patent 3,598,122) and Kochinke (U.S. Patent 5,350,581) cited previously by the Examiner are also unrelated to fentanyl patches.

Finally, teachings of the newly cited reference, Grond et al., relate to iontophoretic transdermal application of

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opioids as described on page 60, lines 26-28. The instant specification clearly distinguishes the transdermal preparations of the present invention from these ion-pair-type adhesive patches.

Thus, the cited combinations of references fail to establish a prima facie case of obviousness with respect to the instant claimed invention as they provide no reasonable expectation of success that an adhesive patch with no sodium acetate could be used to maintain long-term drug efficacy of fentanyl for more than 48 hours.

Withdrawal of all rejections under 35 U.S.C. 103(a) is therefore respectfully requested.

### **III. Supplemental IDS**

Applicants are submitting herewith a Supplemental Information Disclosure Statement with references.

### **IV. Conclusion**

Applicants believe that the foregoing comprises a full and complete response to the Office Actions of record.



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Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

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